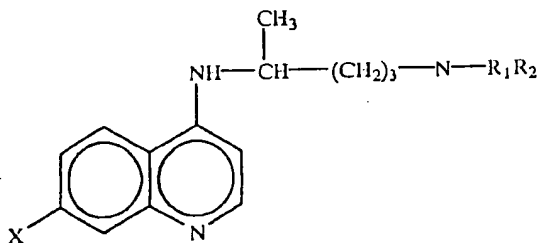


**In the claims:**

**Claim 1 (currently amended)**      A complex comprised of at least one negatively charged nucleic acid and at least one positively charged polymeric conjugate with the bond therebetween being electrostatic in nature, the polymeric conjugate containing a polylysine formed from monomers having free  $\text{NH}_3^+$  groups, at least 10% of free  $\text{NH}_3^+$  groups of the said polylysine are substituted by residues which are protonated in a weakly acid medium causing destabilization of cell membranes, and optionally at least one free  $\text{NH}_3^+$  group of the said polylysine is substituted by a molecule with a recognition signal recognized by a cell membrane receptor, with the proviso that all the free  $\text{NH}_3$  groups of the said polylysine make up at least 30% of the number of monomers of the skeleton of the polymeric conjugate wherein said residues causing destabilization of cell membrane in a weakly acid medium are selected from the group consisting of family of compounds having an imidazole nucleus, pterines, pyridines and quinolines of the formula:



in which R<sub>1</sub> is hydrogen, R<sub>2</sub> is  $-(CH_2)_n-CO_2-H_2-X$  is hydrogen or chlorine and n is an integer from 1 to 10, wherein said recognition signal is selected from the group consisting of:

- a) simple osides selected from the group consisting of a  $\alpha$  or  $\beta$  conformers of 2-deoxy, 2-aminoor 2-deoxy, 2-~~acetamide~~ acetamido neutral monosaccharides;  $\alpha$  or  $\beta$  conformers of glycuronic acid derivatives of neutral monosaccharides,  $\alpha$  or  $\beta$  conformers of L-iduronic acid, of keto-deoxy-octonic acid, of N-acetyl neuraminic acid or of N-glycoloyl-neuraminic acid; and  $\alpha$  or  $\beta$  conformers of neutral 6-deoxy monosaccharides;
- b) a disaccharide selected from the group consisting of lactose and mannopyranosyl  $\alpha$ -6-mannopyranose,
- c) complex osides selected from the group consisting of Lewis<sup>a</sup>, Lewis<sup>b</sup>, Lewis<sup>x</sup>, oligomannosides and ~~oligolactisoamines~~ oligolactosamines and
- d) peptides.

**Claim 2 (currently amended)**      The complex of claim 1 wherein ~~said~~ the residues causing destabilization of cell membrane in a weakly acid medium are quinolines ~~are~~ selected from the group consisting of 7-chloro-4-(amino-1-methyl-butylamino)-quinoline, N<sup>4</sup>-~~(7-~~the group consisting of (7-chloro-4-(amino-1-methyl-butylamino)-quinoline, ~~chloro-4-quinoliny]~~ 1,4-pentanediamine, 8-(4-amino-1-methylbutylamino)-6-methoxyquinoline (primaquine), N<sup>4</sup>-~~(6-methoxy-8-quinoliny]~~ 1,4-pentanediamine, N<sup>4</sup>-(7-chloro-4-quinoliny] 1,4-pentanediamine, 8-(4-amino-1-methyl-butylamino)-6-methoxyquinoline (primaquine), and N<sup>4</sup>-(6-methoxy-8-quinoliny] 1,4-

pentane-diamine, histidine, (compound carrying an imidazole nucleus) and pyridines selected from the group consisting of nicotinic acid and quinolenic acid ~~and pterines~~.

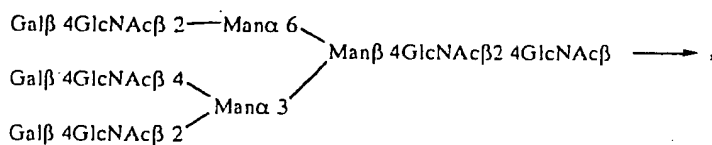
**Claim 3** (previously presented)      The complex of claim 1 wherein the free  $\text{NH}_3^+$  groups of the polylysine are substituted with a non-charged gluconyl residue causing a reduction in the positive charge of the polymeric conjugate which facilitates salting out of the nucleic acids upon dissociation of the complex.

**Claim 4** (previously presented)      The complex of claim 1 wherein recognition-signal is a peptide chosen from the group consisting of

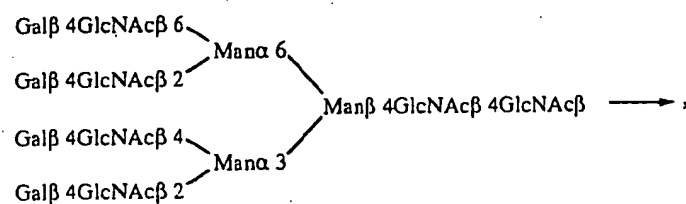
- (a) anti-inflammatory peptides recognized by receptors of the vascular wall,
- (b) ligand peptide of integrins,
- (c) chemiotactic factors and
- (d) peptides hormones.

**Claim 5** (previously presented)      The complex of claim 1 wherein:  
the monosaccharide are selected from the group consisting of galactose, mannose, fucose, glucose, ribose, xylose and rhamnose and  
the complex osides are selected from the group consisting of

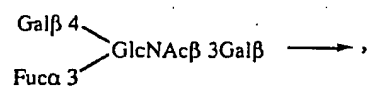
- (a) Asialo-oligoside of the type of triantennar lactosamine of



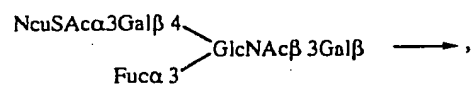
- (b) Asialo-oligoside of the type of tetraantennar lactosamin of the formula



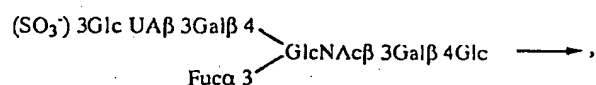
(c) Lewis x of the formula



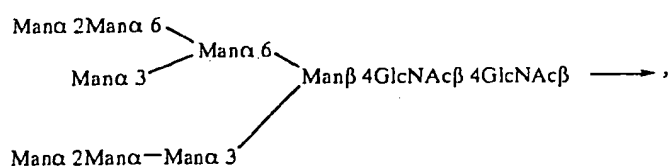
(d) Lewis x sialyl of the formula



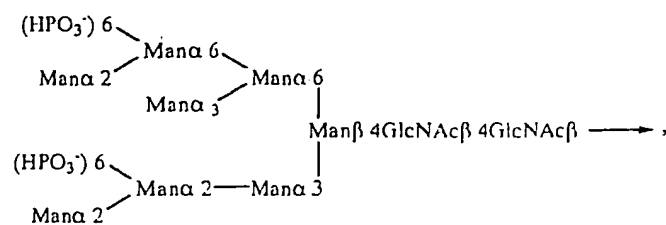
(e) Sulphated Lewis x derivative (HNK1) of the formula



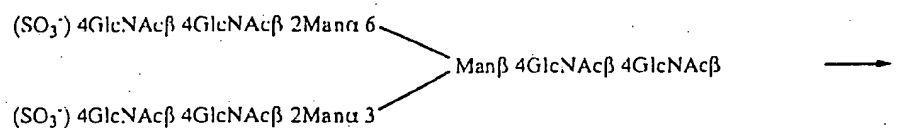
(f) Oligomannoside of the formula



(g) Phosphorylated oligomannoside



(h) Oligosaccharide of the type of sulphated lactosamine of the formula



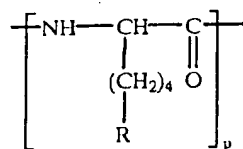
- i. Lactose,
- j.  $\text{Fuc}\alpha 2\text{Gak}\beta 3$  ( $\text{fuc}\alpha 4$ )  $\text{GlcNAc}\beta 1\text{Gal}\beta 3\text{Glc}$ ,
- k.  $\text{Fuc}\alpha 4$  ( $\text{Ga}\beta 3$ )  $\text{GlcNAc}\beta 3\text{Gal}\beta$  and
- l.  $\text{Man}\alpha 6\text{-man}$ .

**Claim 6** (previously presented)      The complex of claim 5 wherein the peptides are selected from the group consisting of

Vasodilar intestinal polypeptide (VIP)

HSDAVFTDNYTRLRKQMAVKKYLNSILN-NH<sub>2</sub> (SEQ ID No: 2)  
atrial natriuretic polypeptide (ANP)  
SLRRSSCFGGRMDRIGAQSGLGCNSFRY (SEQ ID No: 3)  
lipocortin  
HDMNKVLDL (SEQ ID No: 4)  
bradykinin  
RPPGFSPER (SEQ ID No: 5);  
peptides of integrins, peptide hormones and chemotactics factors.

**Claim 7** (previously presented)      The complex of claim 1 wherein the polymeric conjugate has the formula:



wherein

p is an integer from 15 to 900,

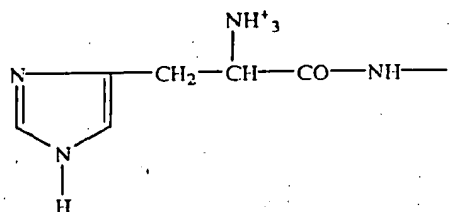
10 to 45% of the radical R being a residue with an imidazole nucleus,

10 to 90% of R being free  $\text{NH}_3^+$  groups,

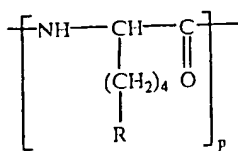
and optionally 0 to 45% of R being  $-\text{NH}-\text{CO}-(\text{CHOH})_m-\text{R}_1$ , m is an integer from

2 to 15 and  $\text{R}_1$  is hydrogen or alkyl of 1 to 15 carbon atoms.

**Claim 8** (previously presented)      The complex of claim 7 wherein R is a residue with an imidazole nucleus of the formula:



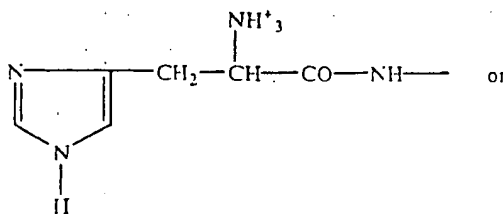
**Claim 9** (previously presented)      The complex of claim 7 wherein the polymeric conjugate has the following formula:



wherein

p is an integer from 15 to 900,

10% to 45% of R is a residue having an imidazole nucleus and optionally a free  $\text{NH}_3^+$ , R has the formula:



with the proviso that all the free  $\text{NH}_3^+$  functions make up at least 30% of the number of monomer units of the polymeric skeleton of the above mentioned polymeric conjugate.

**Claim 10** (previously presented) A complex according to claim 1 wherein the nucleic acid is selected from the group consisting of:

- a) marker genes and
- b) genes encoding a therapeutic protein.

**Claim 11** (previously presented) Positively charged polymeric conjugate containing a polylysine formed from monomers having free  $\text{NH}_3^+$  groups:

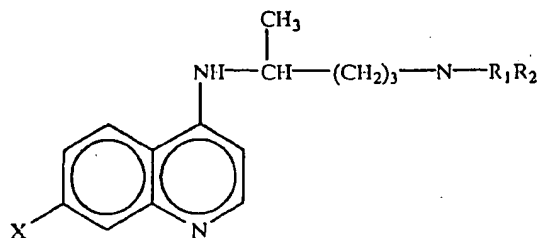
at least 10% of the free  $\text{NH}_3^+$  groups of the said polylysine are substituted by residues which are protonated in a weakly acid medium causing destabilization of cell membranes,

and optionally some of the free  $\text{NH}_3^+$  groups of the said polylysine can be substituted by a molecular with a recognition signal recognized by a cell membrane receptor.

with the proviso that all the free  $\text{NH}_3^+$  groups of the said polylysine make up at least 30% of the number of monomers of the skeleton of the polymeric conjugate,

wherein said residues causing destabilization of cell membranes in a weakly acid

medium; are selected from the group consisting of family of compounds having an imidazole nucleus, pterines, pyridines and quinolines of the formula



in which  $R_1$  is hydrogen,  $R_2$  is hydrogen,  $R_2$  is  $(CH_2)_n-CO_2-H_2X$  is hydrogen or chlorine and  $n$  is an integer from 1 to 10, wherein said recognition signal is selected from the group consisting of:

simple osides selected from the group consisting of  $\alpha$  or  $\beta$  conformers of 2-deoxy, of 2-amino or of 2-deoxy, 2-acetamido neutral monosaccharides;  $\alpha$  or  $\beta$  conformers of glycuronic acid derivatives of neutral monosaccharides;  $\alpha$  or  $\beta$  conformers of 1-iduronic acid, of keto-deoxy-octonic acid, of M-acetyl-neuraminic acid, or of N-glycoloyl-neuraminic acid, and  $\alpha$  or  $\beta$  conformers of neutral 6-deoxy monosaccharides;

a disaccharide selected from the group consisting of lactose and mannopyranosyl  $\alpha$ -6-mannopyranose,

and a complex osides selected from the group consisting of Lewis<sup>a</sup>, Lewis<sup>b</sup>, Lewis<sup>x</sup>, oligomannosides and oligolactosamines and peptides.

**Claim 12** (previously presented)      The positively charged polymeric conjugate



according to claim 11 wherein the free  $\text{NH}_3^+$  groups of the said polylysine are substituted with a non-charged residue causing a reduction in the positive charge of the polymeric conjugate which facilitates salting out of the nucleic acids upon dissociation of the complex, said non-charged residue being a gluconyl.

**Claim 13** (previously presented)      The composition comprising the complex of claim 1 and an inert pharmaceutical carrier.

**Claim 14** (currently amended)      A method of transfecting cultured cells comprising incubating said cells in the presence of the composition of claim 13 under conditions wherein said composition enter said ~~said~~ cells, and the nucleic acid comprised in the complex of said composition is released to transfect cultured cells.

**Claim 15** (previously presented)      The method of claim 14 wherein the cells are selected from the group consisting of

cells of hematopoietic strains;c

dendritic cells;

liver cells;

skeletal muscle cells;

skin cells;

fibroblasts,

keratinocytes,

dendritic cells,

melanocytes;

cells of the vascular walls  
endothelial;  
smooth muscle  
epithelial cells of the respiratory tract;  
cells of the central nervous system;  
cancerous cells; and  
cells of the immune system.

**Claim 16** (currently amended)      The complex of claim 1 wherein the residue causing destabilization of cell membrane in a weakly acid medium is alkylimidazole of 1 to 10 alkyl carbon atoms.